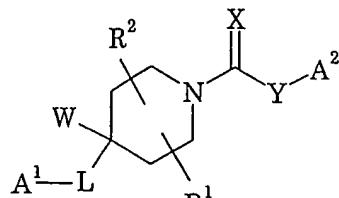


CLAIMS

1. A compound of formula (I):

5



(I)

wherein:

A<sup>1</sup> is phenyl, a six-membered aromatic heterocycle containing one, two or  
10 three nitrogen atoms, or a five-membered aromatic heterocycle containing up to  
four heteroatoms chosen from O, N and S, at most one heteroatom being O or S;  
A<sup>1</sup> is unsubstituted or substituted by one, two or three substituents  
independently chosen from halogen, C<sub>1</sub>-alkyl, C<sub>2</sub>-alkenyl, C<sub>2</sub>-alkynyl,  
haloC<sub>1</sub>-alkyl, C<sub>1</sub>-alkoxy, haloC<sub>1</sub>-alkoxy, hydroxy, cyano, nitro and amino;  
15 A<sup>2</sup> is phenyl, a six-membered aromatic heterocycle containing one, two or  
three nitrogen atoms, or a five-membered aromatic heterocycle containing up to  
four heteroatoms chosen from O, N and S, at most one heteroatom being O or S;  
A<sup>2</sup> is unsubstituted or substituted by one, two or three groups  
independently chosen from halogen, cyano, nitro, amino, C<sub>1</sub>-alkylamino,  
20 di(C<sub>1</sub>-alkyl)amino, C<sub>1</sub>-alkyl C<sub>2</sub>-alkenyl, C<sub>2</sub>-alkynyl, haloC<sub>1</sub>-alkyl, hydroxy,  
C<sub>1</sub>-alkoxy, haloC<sub>1</sub>-alkyl, thiol, SF<sub>6</sub>, phenylC<sub>1</sub>-alkyl and phenyl;  
L is a bond or C<sub>1</sub>-alkylene;  
R<sup>1</sup> and R<sup>2</sup> independently chosen from hydrogen and C<sub>1</sub>-alkyl;  
or R<sup>1</sup> and R<sup>2</sup> may, together, form a methylene or ethylene bridge;  
25 W is halogen, C<sub>1</sub>-alkyl, haloC<sub>1</sub>-alkyl, C<sub>1</sub>-alkoxy or haloC<sub>1</sub>-alkoxy;  
X is O, S or NR<sup>3</sup> where R<sup>3</sup> is hydrogen, hydroxy, C<sub>1</sub>-alkoxy, C<sub>1</sub>-alkyl,  
cyano, C<sub>3</sub>-cycloalkyl, a six-membered saturated heterocycle containing one or two  
heteroatoms independently chosen from O, N and S, and R<sup>3</sup> is, if possible,  
optionally substituted by C<sub>1</sub>-alkyl, C<sub>1</sub>-alkoxy, haloC<sub>1</sub>-alkyl, haloC<sub>1</sub>-alkoxy,

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halogen, amino, nitro, hydroxy, phenyl, a six-membered aromatic heterocycle containing up to three nitrogen atoms or a five-membered aromatic heterocycle containing up to four heteroatoms chosen from O, N and S, at most one heteroatom being O or S;

5 or X, together with the atom to which it is attached, and Y, form an unsaturated five-membered ring together with A<sup>2</sup>;

Y is a bond, C<sub>1-4</sub>alkylene, NH or NH(CH<sub>2</sub>)<sub>1-3</sub>;

or a pharmaceutically acceptable salt thereof.

10 2. A compound selected from:

4-fluoro-4-(3-methylpyridin-2-yl)-N-[4-trifluoromethylphenyl]piperidine-1-carboxamide;

4-fluoro-4(pyridin-2-yl)N-[4-trifluoromethylphenyl]piperidine-1-carboxamide;

4-fluoro-4(pyridine-2-yl)N-[4-trifluoromethylbenzyl]piperidine-1-carboxamide;

15 2-{4-fluoro-1-[4-trifluoromethylbenzoyl]piperidin-4-yl}pyridine;

2-(4-fluoro-1-[[4-trifluoromethylphenyl]acetyl]piperidin-4-yl)pyridine;

2-(4-fluoro-1-{3-[4-trifluoromethylphenyl]propanoyl}piperidin-4-yl)pyridine

4-fluoro-4-(1-methyl-1*H*imidazol-2-yl)-N-[4-trifluoromethylphenyl]piperidine-1-carboxamide;

20 4-methoxy-4-pyridin-2-yl-N-[4-trifluoromethylphenyl]piperidine-1-carboxamide;

4-methoxy-4-pyridin-2-yl-N-[4-trifluoromethylbenzyl]piperidine-1-carboxamide;

4-fluoro-N-(4-isopropylphenyl)-4-(3-methylpyridin-2-yl)piperidine-1-carboxamide;

4-fluoro-4-(3-methylpyridin-2-yl)-N{4-[1,2,2,2-tetrafluoro-1-trifluoromethylethyl]phenyl}piperidine-1-carboxamide;

25 N-(4-Tert butylphenyl)-4-fluoro-4-(3-methylpyridin-2-yl)piperidine-1-carboxamide;

4-fluoro-4-(3-methylpyridin-2-yl)-N-[4-(pentafluoro-λ<sup>6</sup>-sulfanyl)phenyl]piperidine-1-carboxamide;

N-(4-Butylphenyl)-4-fluoro-4-(3-methylpyridin-2-yl)piperidine-1-carboxamide;

30 N-(4-Benzylphenyl)-4-fluoro-4-(3-methylpyridin-2-yl)piperidine-1-carboxamide;

5      *N*-biphenyl-4-yl-4-fluoro-4-(3-methylpyridin-2-yl)piperidine-1-carboxamide;  
4-fluoro-4-(3-methylpyridin-2-yl)-*N*-(5-trifluoromethylpyridin-2-yl)piperidine-1-carboxamide;  
4-(3-chloropyridin-2-yl)-4-fluoro-*N*-(4-trifluoromethylphenyl)piperidine-1-  
carboxamide

10     4-fluoro-4-(3-fluoropyridin-2-yl)-*N*-(4-trifluoromethylphenyl)piperidine-1-  
carboxamide;  
4-fluoro-4-(3-methoxypyridin-2-yl)-*N*-(4-trifluoromethylphenyl)piperidine-1-  
carboxamide;

15     4-fluoro-4-(3-methylpyridin-2-yl)-*N*-(4-trifluoromethylphenyl)piperidine-1-  
carbothioamide;  
*N*-cyano-4-fluoro-4-(3-methylpyridin-2-yl)-*N*-(4-trifluoromethylphenyl)piperidine-1-  
carboximidamide;

20     4-fluoro-4-(3-methylpyridin-2-yl)-*N*-(1-phenylpiperidin-4-yl)-*N*-(4-  
trifluoromethylphenyl)piperidine-1-carboximidamide;  
4-fluoro-4-phenyl-*N*-(4-trifluoromethylphenyl)piperidine-1-carboxamide;  
(+/-)-(syn)-4-fluoro-2-methyl-4-(3-methylpyridin-2-yl)-*N*-(4-  
trifluoromethylphenyl)piperidine-1-carboxamide;  
4-(fluoromethyl)-4-pyridin-2-yl-*N*-(4-trifluoromethylphenyl)piperidine-1-  
carboxamide;

25     *syn* and *anti*-3-fluoro-3-pyridin-2-yl-*N*-(4-trifluoromethylphenyl)-8-  
azabicyclo[3.2.1]octane-8-carboxamide & 3-fluoro-3-pyridin-2-yl-*N*-(4-  
trifluoromethylphenyl)-8-azabicyclo[3.2.1]octane-8-carboxamide;  
4-fluoro-4-pyrimidin-2-yl-*N*-(4-trifluoromethylphenyl)piperidine-1-carboxamide;

30     4-fluoro-4-(3-phenylpropyl)-*N*-(4-trifluoromethylphenyl)piperidine-1-carboxamide;  
2-[4-fluoro-4-(3-methylpyridin-2-yl)piperidin-1-yl]-6-trifluoromethyl-1*H*-  
benzimidazole;  
2-(4-fluoro-4-pyridin-2-ylpiperidin-1-yl)-6-(trifluoromethyl)-1*H*-benzimidazole;  
4-fluoro-*N*-(4-trifluoromethylphenyl)-4-[3-trifluoromethylpyridin-2-yl]piperidine-  
1-carboxamide;

35     4-fluoro-*N*-(4-methylphenyl)-4-(3-methylpyridin-2-yl)piperidine-1-carboxamide;  
*N*-(4-ethylphenyl)-4-fluoro-4-(3-methylpyridin-2-yl)piperidine-1-carboxamide;  
*N*-(4-chlorophenyl)-4-fluoro-4-(3-methylpyridin-2-yl)piperidine-1-carboxamide;

4-fluoro-4-(3-methylpyridin-2-yl)-N-[4-trifluoromethoxyphenyl]piperidine-1-carboxamide;

N-(4-cyanophenyl)-4-fluoro-4-(3-methylpyridin-2-yl)piperidine-1-carboxamide;

N-[4-dimethylaminophenyl]-4-fluoro-4-(3-methylpyridin-2-yl)piperidine-1-carboxamide;

and pharmaceutically acceptable salts thereof.

3. A pharmaceutical composition comprising one or more compounds of claim 1 or 2, or pharmaceutically acceptable salts thereof in association with a

10 pharmaceutically acceptable carrier or excipient.

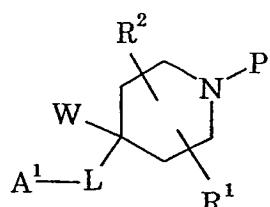
4. A compound of claim 1 or 2, or a pharmaceutically acceptable salt thereof, for use in treatment of the human or animal body.

15 5. The use of a compound of claim 1 or 2, or a pharmaceutically acceptable salt thereof for use in the manufacture of a medicament for the treatment or prevention of physiological disorders that may be ameliorated by modulating VR1 activity.

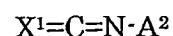
20 6. The use of a compound of claim 1 or 2, or a pharmaceutically acceptable salt thereof for use in the manufacture of a medicament for the treatment or prevention of a disease or condition in which pain and/or inflammation predominates.

25 7. The process for the preparation of a compound of claim 1, which comprises:

(A) for compounds wherein Y is NH or NH(CH<sub>2</sub>)<sub>1-3</sub>, reacting a compound of formula (II) with a compound of formula (III):



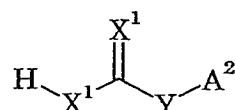
(II)



(III)

wherein  $X^1$  is O or S, P is H or a  $C_1$ -alkoxycarbonyl group such as tert-butoxycarbonyl and  $A^1$ ,  $A^2$ , L,  $R^1$ ,  $R^2$  and W are as defined in claim 1;

5 (B) for compounds wherein Y is a bond or  $C_{1-4}$ alkylene, reacting a compound of formula (II) with a compound of formula (IV):

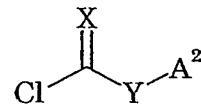


(IV)

10 wherein both  $X^1$ 's are O or S, Y is a bond or  $C_{1-4}$ alkylene and  $A^2$  is as defined in claim 1; or

(C) for compounds wherein X, together with the atom to which it is attached, and Y, form an unsaturated five membered ring together with  $A^2$ , reacting a compound of formula (II) with a compound of formula (V):

15



(V)

wherein X, together with the atom to which it is attached and Y, form an unsaturated five membered ring together with  $A^2$ .

20

8. A method for the treatment or prevention of physiological disorders that may be ameliorated by modulating VR1 activity, which method comprises

administration to a patient in need thereof of an effective amount of a compound of claim 1 or a composition comprising a compound of claim 1.

9. A method for the treatment or prevention of a disease or condition in  
5 which pain and/or inflammation predominates, which method comprises  
administration to a patient in need thereof of an effective amount of a compound  
of claim 1, or a composition comprising a compound of claim 1.

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